ANNEXES (AMENDED SHEETS)

Omit be entered

31. A method according to Claim 30, wherein the solvent includes a so-called intelligent material responsive to a chemical or physical parameter such that each analyte following application to the solid support and drying liquifies in response to said chemical or physical parameter.

32. A method according to any one of Claims 29-31, wherein the analyte is a chemical compound.

33. A method according to any preceding claim, wherein said targets are selected from prokaryotic cells, eukaryotic cells, viruses, molecules, receptors, beads, and combinations thereof.

34. A method according to Claim 33, wherein the targets are cells equipped with reporter functions.

35. A method according to Claim 34, wherein said analyte-target interactions are measurable by the effects of the analytes on the reporter functions of the cells.

36. A method according to any preceding claim, wherein said analyte-target interactions are measured using one or more of the following methods: microscopic, colorimetric, fluorometric, luminometric, densitometric, isotopic, and physical measurements.

37. A method according to any one of Claims 12-36, wherein:

a) a first information carrier, in the form of a film or tape, having analytes to be screened applied to a surface thereof as discrete spots or lines, is brought into contact with a second information carrier, which carrier is also in the form of a film or tape, having targets of interest embedded in a semi-solid matrix on a surface thereof;

b) the respective carriers are wound with their respective analyte- and target-bearing surfaces in contact;

c) the wound carriers are incubated under conditions at which the analytes are released from the first carrier to the target-bearing surface;

d) the first and second carriers are unwound; and

e) the second information carrier is passed to an analysis and information reading unit.

38. A method for the rapid screening of analytes which comprises:

a) bringing a first information carrier, in the form of a film or tape, having analytes to be screened applied to a surface thereof as discrete spots or lines, into contact with a second information carrier, which carrier is also in the form of a film or tape, having targets of interest embedded in a semi-solid matrix on a surface thereof;

b) winding the respective carriers with their respective analyte- and target-bearing surfaces in contact;

c) incubating the wound carriers under conditions at which the analytes are released from the first carrier to the target-bearing surface;

d) unwinding the first and second carriers; and

e) passing the second information carrier to an analysis and information reading unit.

39. An apparatus comprising:

a) an array of capillary tubes from which tubes analytes can be simultaneously released to a surface of a solid support, said support being movable relative to the array; and

b) a housing adapted to receive the array, said housing being connected to an air pump capable of expelling the analytes from their respective capillary tubes onto the solid support by means of a pressure change.

40. An apparatus according to Claim 39, wherein said analytes are in liquid form.

41. A method according to Claim 1, substantially as hereinbefore described with reference to and as illustrated in the accompanying drawings.

42. A method according to Claim 1, substantially as hereinbefore described with reference to the accompanying Examples.

43. A method according to Claim 38, substantially as hereinbefore described and exemplified.

44. An apparatus according to Claim 39, substantially as hereinbefore described with particular reference to and as illustrated in Fig. 20 of the accompanying drawings.

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

ANNE RYAN & CO.
60 Northumberland Road
Ballsbridge
Dublin 4
IRLANDE

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT
(PCT Rule 71.1)

Date of mailing *(day/month/year)*	15.01.2001
Applicant's or agent's file reference: P98-168-PCT	**IMPORTANT NOTIFICATION**

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/IB98/01399	08/09/1998	08/09/1998

Applicant: TIBOTEC N.V. et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/	Authorized officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Pedersen, C Tel.+49 89 2399-8063

Form PCT/IPEA/416 (July 1992)

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
P98-168-PCT		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/IB98/01399	08/09/1998	08/09/1998
International Patent Classification (IPC) or national classification and IPC G01N33/543		
Applicant TIBOTEC N.V. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 8 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 10 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☒ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
17/02/2000	15.01.2001
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Luis Alves, D Telephone No. +49 89 2399 8695

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/IB98/01399

I. Basis of the report

1. This report has been drawn on the basis of *(substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments (Rules 70.16 and 70.17).)*:
Description, pages:

1-3,5-7,10-28	as originally filed			
4	as received on	09/10/2000	with letter of	06/10/2000
8,9	as received on	28/11/2000	with letter of	24/11/2000

Claims, No.:

1-12,13 (part), 32-43	as received on	09/10/2000	with letter of	06/10/2000
13 (part),14-31	as received on	28/11/2000	with letter of	24/11/2000

Drawings, sheets:

1/22-22/22	as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   - ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
   - ☐ the language of publication of the international application (under Rule 48.3(b)).
   - ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   - ☐ contained in the international application in written form.
   - ☐ filed together with the international application in computer readable form.
   - ☐ furnished subsequently to this Authority in written form.
   - ☐ furnished subsequently to this Authority in computer readable form.
   - ☐ The statement that the subsequ ntly furnished written sequenc listing does not go beyond the disclosur in the international application as filed has been furnish d.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 40-43.

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 42, 43 are so unclear that no meaningful opinion could be formed (*specify*):
see separate sheet

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 40, 41.

2. A meaningful international preliminary examination report cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ th written form has not been furnished or do s not comply with the standard.
☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	2, 3, 5-7, 10-27, 30, 33, 34, 36, 37
	No:	Claims	1, 4, 8, 9, 28, 29, 31, 32, 35, 38, 39
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-39
Industrial applicability (IA)	Yes:	Claims	1-39
	No:	Claims	

2. Citations and explanations
see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

Reference is made to the following documents:

D1: WO-A-97/16569
D3: US-A-5 011 779
D4: WO-A-95/11450
D6: SIGAL, NOLAN H. ET AL: 'Approaches and technologies for screening large combinatorial libraries' , COMB. CHEM. MOL. DIVERSITY DRUG DISCOVERY (1998-09-15), 433-443. EDITOR(S): GORDON, ERIC M.;KERWIN, JAMES F., JR. PUBLISHER: WILEY-LISS, NEW YORK, N Y.

D3 and D4 have not been cited in the International search report.

Section III:

1. The subject-matter of claims 40 and 41 (originally filed claims 37 and 38, respectively) has not been searched. Consequently, no opinion will be established on the subject-matter of said claims (Rule 66.1(e) PCT).

2. The subject-matter of claims 42 and 43 lacks characterising features. Said claims do not comply with the requirements of Article 6 PCT and Rule 6.2(a) PCT. It is not possible to establish an opinion on the subject-matter of said claims.

Section V:

1. D1 discloses simultaneous screening of a plurality of compounds by providing a plurality of solid supports, each comprising one of the compounds to be screened, and contacting said supports with a colloidal matrix, into which the compounds may diffuse and contact the target (see p.3, lines 1 to 22). The solid supports comprising the compounds are preferably beads. The colloidal matrix is for example agarose. A diffusion gradient is created when the compounds are released onto the matrix (p.4, lines 10 to 21).

The plurality of beads, containing the corresponding plurality of compounds, can be applied onto the surface of a film, and the film applied to the matrix (see p.10, last paragraph to p.11, first paragraph).

D1 discloses the simultaneous application of analytes to a support, which analytes have been previously individually bound to a plurality of beads.
Present claim 1 is distinguished from D1, which is considered to represent the closest prior art, in that the analytes are applied simultaneously and directly from their respective containers onto the solid support.
Thus the problem to be solved by present claim 1 may be seen as the provision of a simplified method of handling and screening a plurality of analytes.
However, since apparatuses for the simultaneous application of a plurality of samples to a solid support are already known (for example from any of D3 and D4), the solution provided in present claim 1 appears to be obvious. Thus, the subject-matter of claim 1 appears to lack an inventive step over D1 in combination with any of D3 or D4 (Article 33(3) PCT).

The features in claims 4 to 11, 21 to 25 , 28, 31, 32 and 35 are already known from D1. Therefore said claims do not comply with the requirements of Article 33(3) PCT.
Since D1 already discloses the use of films as carriers, the steps defined in dependent claim 36 do not seem to involve an inventive step either (Article 33(3) PCT).
Independent claim 37, which does not define the step of simultaneous and direct application of the analytes to the solid support comprised in claim 1, defines the steps of contacting the analyte and target carriers. As for claim 36, these steps do not seem to involve an inventive step over D1 (Article 33(3) PCT).
The features in dependent claims 2, 3, 12 to 20, 26, 27, 29, 30, 33 and 34 are not specifically disclosed in D1. However, said features appear to be well known possibilities and do not seem to render inventive the subject-matter of said claims (Article 33(3) PCT).

2. D3 discloses an apparatus for simultaneously dispensing a plurality of liquid samples onto a solid support (a multichannel pipette) (see abstract and column 3, second paragraph). The apparatus disclosed in D3 is considered to fall within the scope of

present claim 38 because there are capillary pipette tips, although D3 does not specify the ones used. Therefore, it is considered that the apparatus disclosed in D3 comprises multiple capillaries. Thus, the subject-matter of claims 38 and 39 does not comply with the requirements of Article 33(2) PCT.
D3 also discloses methods comprising the simultaneous application of a plurality of samples to a solid support and contacting said solid support with a liquid sample comprising the targets (see column 6, line 43 to column 7, last paragraph). Thus, D3 discloses methods falling within the scope of present claims 1, 4, 8, 9, 28, 29, 31, 32 and 35 (Article 33(2) PCT).

The apparatus in present claim 38 is distinguished from the apparatus disclosed in D4 by the type of pump used (a peristaltic pump). However, this feature does not provide the solution to any problem other than providing an alternative to the known apparatus. The solution to such problem is however obvious since an air pump is a known equivalent to the peristaltic pump disclosed in D4.
Although present claim 38 refers to the relative movement of the solid support and the array of tubes, which in the apparatus disclosed in D4 is the movement of the array of tubes, these feature also does not seem to solve in an inventive way any technical problem because in D4 the two parts were already movable relative to each other.
Therefore, the subject-matter of claims 38 and 39 does not seem to involve an inventive step over D4 (Article 33(3) PCT).

3. Document D6, cited in the International search report as a P-document, has been published seven days after the filing date of the present application and is therefore not considered to be comprised in the state of the art for the purposes of article 33(2) and (3) PCT.

Section VII:

1. Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the documents D1, D3 and D4 is not mentioned in the description, nor are these documents identified therein.

Secti n VIII:

1. The relative term "substantially" used in claim 5 has no well-recognised meaning and leaves the reader in doubt as to the meaning of the technical features to which it refers, thereby rendering the definition of the subject-matter of said claim unclear (Article 6 PCT).

Disclosure of Invention

The invention provides a method for the rapid screening of analytes, comprising the steps of:

a) disposing a plurality of analytes to be screened within individually identifiable containers for storage;

b) simultaneously applying said plurality of analytes onto one or more solid support(s) such that said analytes are directly applied from said containers to the or each solid support and remain isolated from one another;

c) contacting said analyte-carrying solid support(s) with targets provided in a semi-solid or liquid medium, whereby said analytes are released from the solid support(s) to the targets; and

d) measuring analyte-target interactions.

The method according to the invention allows for the manipulation of thousands of different analytes simultaneously.

Step a) of the method according to the invention ensures that the analytes are transferred from the containers to the solid support(s) in such a manner as to maintain the transferred contents of each container separate from those of each other container.

The individually identifiable containers are preferably selected from tubes, including capillary tubes, pens, including plotter pens, and print heads or any container allowing for the storage and direct application of an analyte from the container to a given solid support.

Further, preferably, the individually identifiable containers are an array of capillary tubes each of which is identifiable according to its position within the array, and wherein transfer of the analytes to the solid support(s) occurs by dispensing thereof through the open ends of the capillary tubes.

Claims: -

1. A method for the rapid screening of analytes, comprising the steps of:

a) disposing a plurality of analytes to be screened within individually identifiable containers for storage;

b) simultaneously applying said plurality of analytes onto one or more solid support(s) such that said analytes are directly applied from said containers to the or each solid support and remain isolated from one another;

c) contacting said analyte-carrying solid support(s) with targets provided in a semi-solid or liquid medium, whereby said analytes are released from the solid support(s) to the targets; and

d) measuring analyte-target interactions.

2. A method according to Claim 1, wherein the individually identifiable containers are selected from tubes, including capillary tubes, pens, including plotter pens, and print heads.

3. A method according to Claim 2, wherein the individually identifiable containers are an array of capillary tubes each of which is identifiable according to its position within the array, and wherein transfer of the analytes to the solid support(s) occurs by dispensing thereof through the open ends of the capillary tubes.

4. A method according to any one of Claims 1-3, wherein the solid support is of a substantially flat, disc-, rectangular- or square-shape.

5. A method according to Claim 4, wherein the solid support comprises a material which allows for spontaneous release of the analyte(s) when applied thereto.

6. A method according to Claim 4, wherein the solid support comprises a material which allows for controlled release of the analyte(s) when applied thereto.

7. A method according to Claim 5 or 6, wherein said material is said semi-solid medium.

8. A method according to any preceding claim, wherein when each analyte is applied to the solid support it diffuses thereon so as to produce a concentration gradient.

9. A method according to any preceding claim, wherein the surface of the solid support onto which the analytes are applied is selected from polymers, ceramics, metals, cellulose and glass.

10. A method according to any preceding claim, wherein said semi-solid medium is disposed on a carrier.

11. A method according to Claim 10, wherein the solid support is in the form of a flexible film or tape onto which the target-containing semi-solid medium is applied, whereby the method can be automated using a system of rollers to progress the flexible film or tape through the various steps of the method.

12. A method according to Claim 11, wherein the carrier is covered by a further layer of film or tape and is thereby sandwiched between the solid support and the covering layer.

13. A method according to Claim 11 or 12, wherein the solid support or covering layer (if present) is provided with a track for the recordal of information regarding the applied analytes, whereby the

information can be read and processed simultaneously with the measurement of analyte-target interactions in an automated process.

14. A method according to any one of Claims 1-9, wherein the solid support is itself a detector or forms part of a detector.

15. A method according to Claim 14, wherein the solid support is selected from a SiO_2 wafer, a charge-coupled device, and a photographic film.

16. A method according to any preceding claim, wherein the surface of the solid support is coated with a membrane, a molecular monolayer, a cellular monolayer or a Langmuir-Blodgett film.

17. A method according to any preceding claim, wherein the solid support is itself an information carrier which carries information in electronic, magnetic or digitised form.

18. A method according to any preceding claim, wherein said surface of the solid support is reflective.

19. A method according to Claim 18, when dependent on Claim **16**, wherein said surface is the reflective surface of a compact disc.

20. A method according to Claim 19, further comprising the step of copying said compact disc to a writable compact disc.

21. A method according to any preceding claim, wherein the semi-solid medium comprises a substance which provides a semi-solid or viscous liquid environment allowing controlled release of said anlaytes to said target.

22. A method according to Claim 21, wherein said substance is selected from gelatin, polysaccharides such as agar and agarose, and polymers such as methylcellulose and polyacrylamide or a so-called intelligent material.

23. A method according to any preceding claim, wherein steps **b**) and **c**) are carried out simultaneously.

24. A method according to Claim 1, wherein each analyte is applied to a single solid support.

25. A method according to Claim 24, wherein the solid support is of a rod shape or a spherical shape.

26. A method according to Claim 24 or 25, wherein each analyte-bearing solid support is contacted in step b) with a target in a separate compartment of a multi-compartmented apparatus.

27. A method according to Claim 26, wherein said compartments are an arrangement of mini-wells in said apparatus.

28. A method according to any preceding claim, wherein the analytes are selected from chemical compounds, antigens, antibodies, DNA-probes, cells and beads and liposomes carrying an analyte of interest.

29. A method according to Claim 28, wherein the analytes, when applied to the solid support, are dissolved in an organic or inorganic solvent.

30. A method according to Claim 29, wherein the solvent includes a so-called intelligent material responsive to a chemical or physical parameter such that each analyte following application to the solid support and drying liquifies in response to said chemical or physical parameter.

31. A method according to any one of Claims 28-30, wherein the analyte is a chemical compound.

32. A method according to any preceding claim, wherein said targets are selected from prokaryotic cells, eukaryotic cells, viruses, molecules, receptors, beads, and combinations thereof.

33. A method according to Claim 32, wherein the targets are cells equipped with reporter functions.

34. A method according to Claim 33, wherein said analyte-target interactions are measurable by the effects of the analytes on the reporter functions of the cells.

35. A method according to any preceding claim, wherein said analyte-target interactions are measured using one or more of the following methods: microscopic, colorimetric, fluorometric, luminometric, densitometric, isotopic, and physical measurements.

36. A method according to any one of Claims 11-35, wherein:

a) a first information carrier, in the form of a film or tape, having analytes to be screened applied to a surface thereof as discrete spots or lines, is brought into contact with a second information carrier, which carrier is also in the form of a film or tape, having targets of interest embedded in a semi-solid matrix on a surface thereof;

b) the respective carriers are wound with their respective analyte- and target-bearing surfaces in contact;

c) the wound carriers are incubated under conditions at which the analytes are released from the first carrier to the target-bearing surface;

d) the first and second carriers are unwound; and

e) the second information carrier is passed to an analysis and information reading unit.

37. A method for the rapid screening of analytes which comprises:

a) bringing a first information carrier, in the form of a film or tape, having analytes to be screened applied to a surface thereof as discrete spots or lines, into contact with a second information carrier, which carrier is also in the form of a film or tape, having targets of interest embedded in a semi-solid matrix on a surface thereof;

b) winding the respective carriers with their respective analyte- and target-bearing surfaces in contact;

c) incubating the wound carriers under conditions at which the analytes are released from the first carrier to the target-bearing surface;

d) unwinding the first and second carriers; and

e) passing the second information carrier to an analysis and information reading unit.

38. An apparatus comprising:

a) an array of capillary tubes from which tubes analytes can be simultaneously released to a surface of a solid support, said support being movable relative to the array; and

b) a housing adapted to receive the array, said housing being connected to an air pump capable of expelling the analytes from their respective capillary tubes onto the solid support by means of a pressure change.

39. An apparatus according to Claim 38, wherein said analytes are in liquid form.

40. A method according to Claim 1, substantially as hereinbefore described with reference to and as illustrated in the accompanying drawings.

41. A method according to Claim 1, substantially as hereinbefore described with reference to the accompanying Examples.

42. A method according to Claim 37, substantially as hereinbefore described and exemplified.

43. An apparatus according to Claim 38, substantially as hereinbefore described with particular reference to and as illustrated in Fig. 20 of the accompanying drawings.

The surface of the solid support can be coated with a membrane, a molecular monolayer, a cellular monolayer or a Langmuir-Blodgett film.

All of these coatings can be used to control the release of analytes when applied thereto.

In another embodiment, the solid support is itself an information carrier which carries information in electronic, magnetic or digitised form.

In an alternative embodiment, the surface of the solid support is reflective. For example, the surface can be the reflective surface of a compact disc.

The method according to the invention can further comprise the step of copying said compact disc to a writable compact disc.

In another embodiment, the semi-solid medium comprises a substance which provides a semi-solid or viscous liquid environment allowing controlled release of said **analytes** to said target.

Preferably, the substance which provides a semi-solid or viscous liquid environment is selected from gelatin, polysaccharides such as agar and agarose, and polymers such as methylcellulose and polyacrylamide or a so-called intelligent material. Such substances can also be used to control the release of the analytes when applied thereto.

So-called intelligent materials are natural and synthetic polymer gels that are undergo phase transitions and critical phenomena, for example phase transitions accompanied by a reversible, discontinuous volume change as large as several hundred times, in response to infinitesimal changes in environmental conditions.

Examples of so-called intelligent materials are polymeric gel-type materials, more particularly hydrogels that can take up a fluid and

subsequently release that fluid in response to a chemical or physical stimulus or trigger. An example of a chemical stimulus is a change of pH or ionic or solvent composition and an example of a physical stimulus is light of a particular wave-length or a laser beam, a change of temperature or a small electric field.

For example, a gel containing N-isopropylacrylamide (main constituent) and the light-sensitive chromophore, the trisodium salt of copper undergoes phase transitions induced by visible light (Suzuki, A. and Tanaka, T (Nature (1990); *346*, *345-347*).

A range of suitable thermo-sensitive polymers is described by Snowden, M.J. *et al.* (Chemistry & Industry (July, 1996); p.p. 531-534.

Other suitable gels are those sold under the Trade Mark THERA GEL marketed by Gel Sciences Inc., Boston, M.A., U.S.A.

In a further embodiment, steps **b)** and **c)** are carried out simultaneously.

In a still further embodiment, each analyte is applied to a single solid support.

In this embodiment, the solid support is preferably of a rod shape or a spherical shape.

Further, preferably each analyte-bearing solid support is contacted in step b) with a target in a separate compartment of a multi-compartmented apparatus, more especially said compartments are an arrangement of mini-wells in said apparatus.

In another preferred embodiment, the analyte containers are small inert solid supports onto the surfaces of which analytes have been applied. Dipping of the solid supports into a liquid phase or semi-solid phase results in time-dependent release of analyte from the solid support into the liquid or semi-solid phase. In this way, dilutions of

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

ANNE RYAN & CO.
60 Northumberland Road
Ballsbridge
Dublin 4
IRLANDE

PCT

NOTIFICATION CONCERNING INFORMAL COMMUNICATIONS WITH THE APPLICANT

(PCT Rule 66.6)

Date of mailing *(day/month/year)* 15.01.2001

Applicant's or agent's file reference
P98-168-PCT

TRANSMITTAL FOR INFORMATION

International application no.
PCT/IB98/01399

International filing date *(day/month/year)*
08/09/1998

Applicant
TIBOTEC N.V. et al.

An informal communication took place on 13/11/2000, between the International Preliminary Examining Authority and the applicant / the agent.

A copy of the note on that communication (Form PCT/IPEA/428) is herewith transmitted for your information.

Name and mailing address of the international preliminary examining authority
European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized officer
Pedersen, C

Telephone No.+49 89 2399-8063

Form PCT/IPEA/429 (july 1993)

Patent Cooperation Treaty
Traît´ d coopération en matièr de brevets

PCT

Application No.: PCT/IB98/01399

Note on an informal communication by telephone with the Applicant

No extension of time limit is granted and the time limit remains as previously set

Participants

Agent: Ryan, A.

Examiner(s): Luis Alves, D

Summary of the communication

The Representative contacted the Examiner with respect to international applicatic PCT/IB98/01399, to ask whether the reply to the first written opinion had already bee examined. The Examiner informed the Representative that said reply had not yet bee examined.

13/11/2000
.....
Date *(day / month / year)*

Luis Alves, D
.....
Authorized officer of IPE

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Assistant Commissioner for Patents
United States Patent and Trademark Office
Box PCT
Washington, D.C.20231
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 17 March 2000 (17.03.00)	
International application No. PCT/IB98/01399	**Applicant's or agent's file reference** P98-168-PCT
International filing date (day/month/year) 08 September 1998 (08.09.98)	**Priority date** (day/month/year)
Applicant PAUWELS, Rudi, Wilfried, Jan et al	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

17 February 2000 (17.02.00)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

S. Mafla

Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	FOR FURTHER ACTION	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
P98-168-PCT		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/IB 98/01399	08/09/1998	
Applicant		
TIBOTEC N.V. et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 5 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

a. With regard to the **language,** the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

[ ] the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

[ ] contained in the international application in written form.

[ ] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority in written form.

[ ] furnished subsequently to this Authority in computer readble form.

[ ] the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

[ ] the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. [X] **Certain claims were found unsearchable** (See Box I).

3. [ ] **Unity of invention is lacking** (see Box II).

4. With regard to the **title,**

[X] the text is approved as submitted by the applicant.

[ ] the text has been established by this Authority to read as follows:

5. With regard to the **abstract,**

[X] the text is approved as submitted by the applicant.

[ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from th date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. 21

[X] as suggested by the applicant.

[ ] None of the figures.

[ ] because the applicant failed to suggest a figure.

[ ] because this figure better characterizes the invention.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB 98/01399

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☒ Claims Nos.: 37,38
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Claims not searched: 37,38

Claims 37 and 38 do not comply with the pescribed requirements of Article 6 and Rule 6.3(a) PCT to such an extent that a meaningful search is not possible. They do no relate to technical features that allow the formulation of a meaningful search.

The applicant's atention is drawn to the fact that claims relating to inventions in respect of wich no international saerch report has been established need not be the subject of an international preliminary examination (rule 66.1(e) PCT). The aplicant is advised that the EPO policy when acting as an International Preliminary Examination Authority is normally not to carry out a preliminary examination on matter wich has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 37,38

Claims 37 and 38 do not comply with the pescribed requirements of Article 6 and Rule 6.3(a) PCT to such an extent that a meaningful search is not possible. They do no relate to technical features that allow the formulation of a meaningful search.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

International Application No
[redacted]/IB 98/01399

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 G01N33/543 B01L3/02 G01N33/569 G01N33/573 C12Q1/18

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 97 16569 A (PHARMACOPEIA INC) 9 May 1997 (1997-05-09) the whole document ---	1,5-11, 15, 22-30, 32-36
Y	US 4 276 048 A (LEABACK DAVID H) 30 June 1981 (1981-06-30) abstract ---	1,5-11, 15, 22-30, 32-36
A	WO 98 01533 A (BURSTEIN LAB INC) 15 January 1998 (1998-01-15) the whole document --- -/--	1,5-11, 15-24, 29-36

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
7 July 1999	20/07/1999

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Gundlach, B

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International Application No
T/IB 98/01399

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
A	WO 98 21571 A (BINDER ANDRES ;CIBA GEIGY AG (CH); EHRAT MARKUS (CH); OROSZLAN PET) 22 May 1998 (1998-05-22) abstract; figure 3 ---	1,5-11, 15-24, 29-36
A	GB 2 008 767 A (DU PONT) 6 June 1979 (1979-06-06) abstract page 1, column 2, line 95 - page 2, column 2, line 101 ---	1,5-19, 22-24, 29-36
A	EKINS R ET AL: "MULTIANALYTE MICROSPOT IMMUNOASSAY. THE MICROANALYTICAL 'COMPACT DISK' OF THE FUTURE" ANNALES DE BIOLOGIE CLINIQUE, vol. 50, no. 5, 1 January 1992 (1992-01-01), pages 337-353, XP000617908 the whole document ---	1,5,10, 15,16
P,X	SIGAL, NOLAN H. ET AL: "Approaches and technologies for screening large combinatorial libraries" , COMB. CHEM. MOL. DIVERSITY DRUG DISCOVERY (1998-09-15), 433-443. EDITOR(S): GORDON, ERIC M.;KERWIN, JAMES F., JR. PUBLISHER: WILEY-LISS, NEW YORK, N Y. XP002108436 the whole document -----	1-3, 5-11,15, 22-30, 32-36

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
[redacted]/IB 98/01399

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9716569 A	09-05-1997	US 5856083 A	05-01-1999
		AU 7553596 A	22-05-1997
US 4276048 A	30-06-1981	NONE	
WO 9801533 A	15-01-1998	AU 3958597 A	02-02-1998
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		FI 783346 A	04-05-1979
		FR 2408142 A	01-06-1979
		IE 47482 B	04-04-1984
		JP 1235938 C	17-10-1984
		JP 54091296 A	19-07-1979
		JP 59012139 B	21-03-1984
		LU 80471 A	15-06-1979
		NL 7810910 A	07-05-1979
		SE 431257 B	23-01-1984
		SE 7810351 A	04-05-1979